Remarks/Arguments

Claims 1, 3-5, and 46-48 are pending in the application. Claim 48 is amended.

Amendments to the specification are to alleviate confusion in the specific embodiment disclosed in the specification calling for application of the chemotherapeutic agent CPT-11. CPT-11 is known by those skilled in the art to be synonymous with irinotecan. Those skilled in the art would also recognize that CPT-11 is not synonymous with cisplatin, as indicated in the disclosure.

In the interests of advancing prosecution of the present invention, Applicant has amended Claim 48 to recite "chimeric 225." Support for the amendment is found, for example, at page 8, lines 10-14 and page 10, lines 10-26 of the specification.

First Rejection Under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the rejection of claims 1, 3-5 and 46-48 under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner continues to assert that what is enabled by the specification is not commensurate with the scope of the claims.

In particular, the Examiner believes that one of ordinary skill in the art would not be convinced that it is possible to treat psoriases by administering an anti-EGFR/HER1 antibody alone because treatment of cancer with a combination of an antibody and a chemotherapeutic agent is more efficient than treatment with an antibody alone.

The rejection is respectfully traversed for the following reasons. First, the Examiner has cited specific passages of references that allegedly support his belief, while ignoring other relevant portions of those references that indicate the use of an antibody alone. Further, the art shows that antibodies alone are useful for treatment of cancer. In addition, one of skill in the art would conclude that it is likely that the psoriasis resolution described in Applicant's disclosure resulted from administration of the anti-EGFR/HER1 antibody, rather than from administration of irinotecan or coadministration of the agents.

The Examiner argues that it is not convincing that treatment is possible with an anti-EGFR antibody alone because studies repeatedly show that treatment with antibodies combined with a chemotherapeutic agent is more efficient than treatment with an antibody

alone. In support of this argument, the Examiner has selectively cited passages from two patent references that suggest that treatment with antibodies combined with a chemotherapeutic agent provides a more efficient treatment than the use of the antibody by itselfand ignored the portions of those references showing that antibodies are useful when administered alone. As noted by the Examiner, U.S. Patent 5,840,301 (Rockwell et al.) discloses that anti-VEGFR antibodies can be combined with a drug such as doxorubicin, cisplatin or taxol. Significantly, the same specification provides extensive evidence, both *in vitro* and *in vivo*, that the antibodies are effective in the absence of a chemotherapeutic agent. For example, the anti-VEGFR antibodies alone neutralize activation of VEGF receptor *in vitro* (col. 14, lines 25-49), and more importantly, significantly reduce tumor growth (col. 17, lines 22-51).

The Examiner has also referred to a single paragraph (0282) of U.S. Patent Application Publication 20030194403 (van de Winkel et al), which discloses coadministration of an anti-EGFR antibody and a therapeutic agent such as cisplatin, and asserted that "[a]ll of the studies in Van de Winkel consist of the administration of anti-EGFR antibodies along with a therapeutic agent, but not anti-EGFR antibodies alone." To the contrary, the Examiner's attention is directed to, for example, paragraphs 0057-0058 and 0279-0280, which disclose the use of anti-EGFR antibodies alone to treat EGFR-related diseases. In those sections, there is no mention or suggestion of co-administration of any other therapeutic agent.

The art shows that antibodies alone are useful for treatment of cancer. The Examiner's attention is respectfully directed to, for example, Cunningham et al., 2004, N. Engl. J. Med. 351:337-45 (Exhibit A), which compares the efficacy of cetuximab in combination with irinotecan with that of cetuximab alone for treatment of metastatic colon cancer that was refractory to treatment with irinotecan. While the response rate of the combination-therapy group was higher than that in the monotherapy group, the authors concluded that cetuximab has clinically significant activity when given alone or in combination with irinotecan. In a second study, cetuximab alone was active in metastatic

colorectal cancer refractory to irinotecan, oxaliplatin, and a fluoropyrinidine (Lenz et al., 2006, J. Clin. Oncol. 24:4914-21; Exhibit B).

One of skill in the art would conclude that it is likely that the psoriasis resolution described in Applicant's disclosure resulted from administration of the anti-EGFR/HER1 antibody, rather than from administration of irinotecan or coadministration of the agents. Long-term resolution of psoriasis in a subject treated for metastatic colon cancer with cetuximab and other chemotherapy agents has been reported by Trivin et al., 2004, Acta Oncologia 43:592-3 (Exhibit C). Prior psoriasis treatments using phototherapy, cortocosteroids, or keratolytic ointment provided only partial and temporary relief. The authors suggested that the complete resolution of psoriasis resulted from inhibition of keratinocytes abnormally stimulated by psoriasis, and stated "it is unlikely that the improvement resulted from the other chemotherapeutic agents or the corticosteroids."

While the Examiner has deemed the Applicant's previous arguments to be unpersuasive, the Examiner's logic is flawed and does not provide a reasonable basis for the position that the pending claims are not enabled. The Examiner's position that claims are not enabled if they do not recite co-administration of CPT-11 is mere supposition. Although the references cited by the Examiner suggest that there is a benefit to coadministration of antibodies and chemotherapeutic agents for treatment of cancer, those references in fact disclose that antibodies alone can be used for treatment, and clinical reports demonstrate the use of antibodies alone for treatment of cancer. More specifically, as demonstrated by Exhibits A and B, anti-EGFR/HER1 antibodies alone are used to treat cancer. With respect to psoriasis, Exhibit C shows that one of skill in the art would conclude that psoriasis can be treated with an anti-EGFR/HER1 antibody alone.

Citing Varani, the Examiner has stated that there are no animal models of psoriasis and asserted that the results provided in Applicant's disclosure are not applicable to any mammal other than humans. The Applicant respectfully points out that the claims recite treatment of a human.

The Applicant requests that the rejection be withdrawn.

Second Rejection Under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the rejection of Claim 48 under 35 U.S.C. 112, first paragraph, asserting that "the specification fails to provide enough information for one of ordinary skill in the art to produce a chimeric antibody with exactly the same characteristics as the C225 antibody, because the specification fails to provide the structure and specific sequence for the claimed C225 antibody."

The rejection is believed moot in view of the amendment to Claim 48. Applicant respectfully requests that the rejection be withdrawn.

Conclusion

It is respectfully submitted that all claims in the present application are in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicant's representative to discuss any issue that would expedite allowance of the subject application.

Respectfully submitted,

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